CLINICAL PRACTICE GUIDELINES, THEIR REPRESENTATION, ENACTMENT AND PROCESSING

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INTRODUCTION

Clinical practice guidelines (CPGs)

Knowledge-based tools for **disease-specific** patient management

[Rosenfeld and Shiffman, 2009]

- Introduced to limit the variations in service delivery and to minimize healthcare costs
- Initially aimed at nurses and other ancillary personnel, then adopted (slowly) by physicians
- Increasing popularity of *computer-interpretable guidelines* (CIGs) integrated with clinical systems

Diversified clinical terminology: guideline, algorithm, pathway…

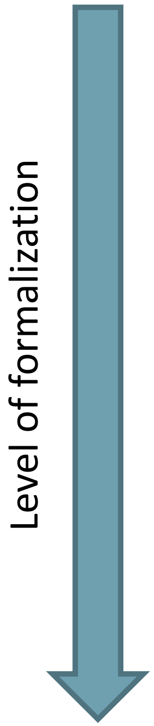
CPGs (and CIGs) in clinical practice

- On the one hand, multiple advantages
  - Increased adoption of evidence-based medicine (EBM) and improved adherence to standards of practice
  - Positive impact on patient outcomes (e.g., decreased mortality)

Clinical guidelines are only one option
for improving the quality of care [Woolf et al., 1999]

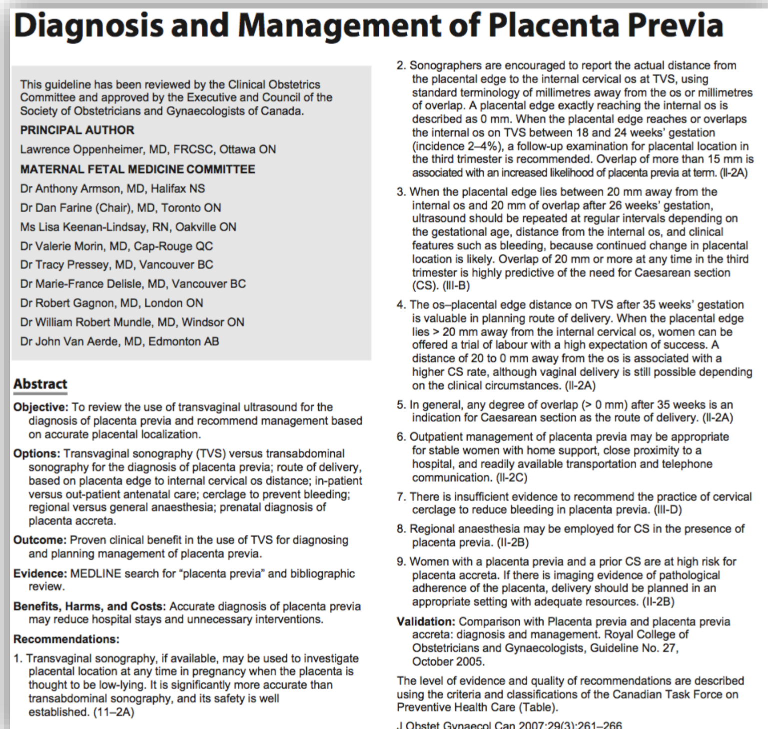
- On the other hand, still limited adoption
  - Considered to be "cookbook medicine"
  - Given mostly in paper format
  - Limited standardization of formal representations
  - **No support for multimorbid conditions**

Representation of CPGs and CIGs



- **Text** models (CPGs)
  - Limited to textual content (possibly long)
  - Additional information (tags) augmenting the text
- **Task-network** models (CIGs)
  - Interpretable by a physician
  - Aimed at (semi-) automatic analysis and enactment by a computer system

Sample CPGs and CIGs



Diagnosis and Management of Placenta Previa

This guideline has been reviewed by the Clinical Obstetrics Committee and approved by the Executive and Council of the Society of Obstetricians and Gynaecologists of Canada.

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Abstract

Objective: To review the use of transvaginal ultrasound for the diagnosis of placenta previa and recommend management based on accurate placental localization.

Options: Transvaginal sonography (TVS) versus transabdominal sonography for the diagnosis of placenta previa; route of delivery, based on placental edge to internal cervical os distance; in-patient versus out-patient antenatal care; cerclage to prevent bleeding; regional versus general anaesthesia; prenatal diagnosis of placenta accreta.

Outcome: Proven clinical benefit in the use of TVS for diagnosing and planning management of placenta previa.

Evidence: MEDLINE search for "placenta previa" and bibliographic review.

Benefits, Harms, and Costs: Accurate diagnosis of placenta previa may reduce hospital stays and unnecessary interventions.

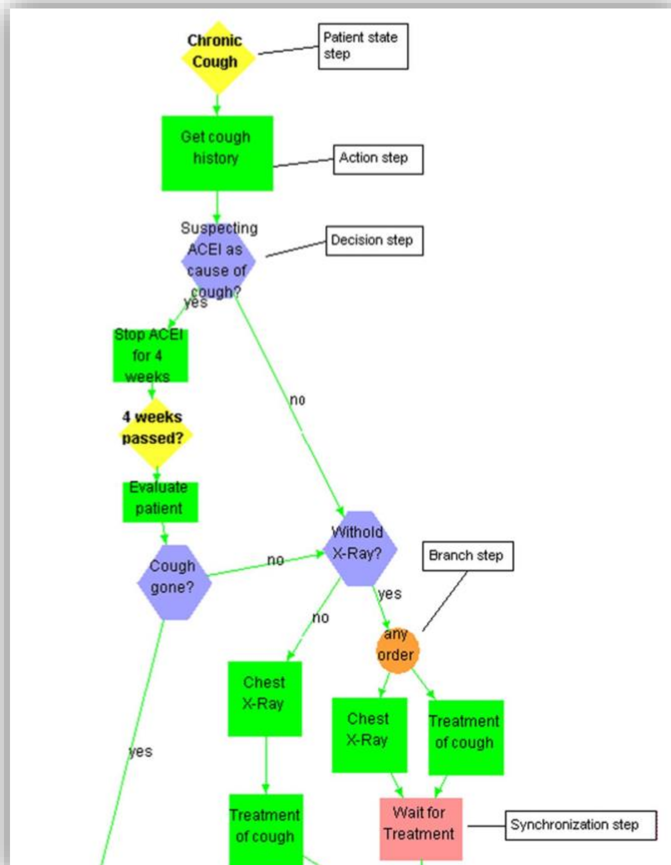
Recommendations:

1. Transvaginal sonography, if available, may be used to investigate placental location at any time in pregnancy when the placenta is thought to be low-lying. It is significantly more accurate than transabdominal sonography, and its safety is well established. (11–2A)
2. Sonographers are encouraged to report the actual distance from the placental edge to the internal cervical os at TVS, using standard terminology of millimetres away from the os or millimetres of overlap. A placental edge exactly reaching the internal os is described as 0 mm. When the placental edge reaches or overlaps the internal os on TVS between 18 and 24 weeks' gestation (incidence 2–4%), a follow-up examination for placental location in the third trimester is recommended. Overlap of more than 15 mm is associated with an increased likelihood of placenta previa at term. (II-2A)
3. When the placental edge lies between 20 mm away from the internal os and 20 mm of overlap after 26 weeks' gestation, ultrasound should be repeated at regular intervals depending on the gestational age, distance from the internal os, and clinical features such as bleeding, because continued change in placental location is likely. Overlap of 20 mm or more at any time in the third trimester is highly predictive of the need for Caesarean section (CS). (III-B)
4. The os–placental edge distance on TVS after 35 weeks' gestation is valuable in planning route of delivery. When the placental edge lies > 20 mm away from the internal cervical os, women can be offered a trial of labour with a high expectation of success. A distance of 20 to 0 mm away from the os is associated with a higher CS rate, although vaginal delivery is still possible depending on the clinical circumstances. (II-2A)
5. In general, any degree of overlap (> 0 mm) after 35 weeks is an indication for Caesarean section as the route of delivery. (II-2A)
6. Outpatient management of placenta previa may be appropriate for stable women with home support, close proximity to a hospital, and readily available transportation and telephone communication. (II-2C)
7. There is insufficient evidence to recommend the practice of cervical cerclage to reduce bleeding in placenta previa. (III-D)
8. Regional anaesthesia may be employed for CS in the presence of placenta previa. (II-2B)
9. Women with a placenta previa and a prior CS are at high risk for placenta accreta. If there is imaging evidence of pathological adherence of the placenta, delivery should be planned in an appropriate setting with adequate resources. (II-2B)

Validation: Comparison with Placenta previa and placenta previa accreta: diagnosis and management. Royal College of Obstetricians and Gynaecologists, Guideline No. 27, October 2005.

The level of evidence and quality of recommendations are described using the criteria and classifications of the Canadian Task Force on Preventive Health Care (Table).

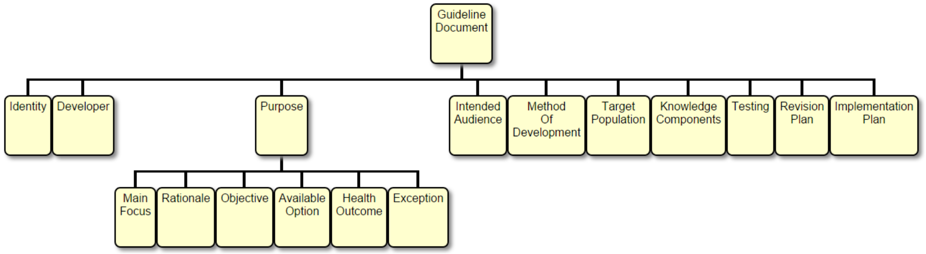
J Obstet Gynaecol Can 2007;29(3):261–266



Text models: GEM (Guideline Elements Model)

http://gem.med.yale.edu

- A set of XML tags (100+) for marking selected parts of a guideline document



- Also a set of tools for viewing and tagging text documents
- Official standard endorsed by ASTM International, very popular, despite its simplicity
- Possibility of automatic discovery of clinical rules – requires more detailed tags (experimental extension)

Task-network models

- A CPG represented as a **directed graph** with nodes capturing specific steps and arcs – dependencies between steps
- Basic types of
  - *Data query* – collecting data (from the user or other system)
  - *Decision* – making a decision
  - *Action* – performing some clinical action
  - *Invocation* – invocation of another CIG
- Multiple representations based on the task-network model with varying complexity and focus (e.g., temporal aspects)
- Increasing popularity due to possible integration with HISs

Task-network model representations

- GLIF3 – a multiple-level representation with conceptual flowcharts and an executable specification
- SAGE – an complete (event-driven) environment for creating and executing CIGs, integration with HIS via vMR
- Asbru – a formalism (+ tools) focused on modeling temporal aspects and uncertainties associated with CIG execution
- PROforma – a formalism (+ tools) for creating and managing CIGs with focus on argumentation-based decision making, one of few commercial applications
- SDA* – a flowchart-based representation developed for the K4CARE project and aimed at team-based automatic execution
- BPMN – a model (+ tools) for representing business processes

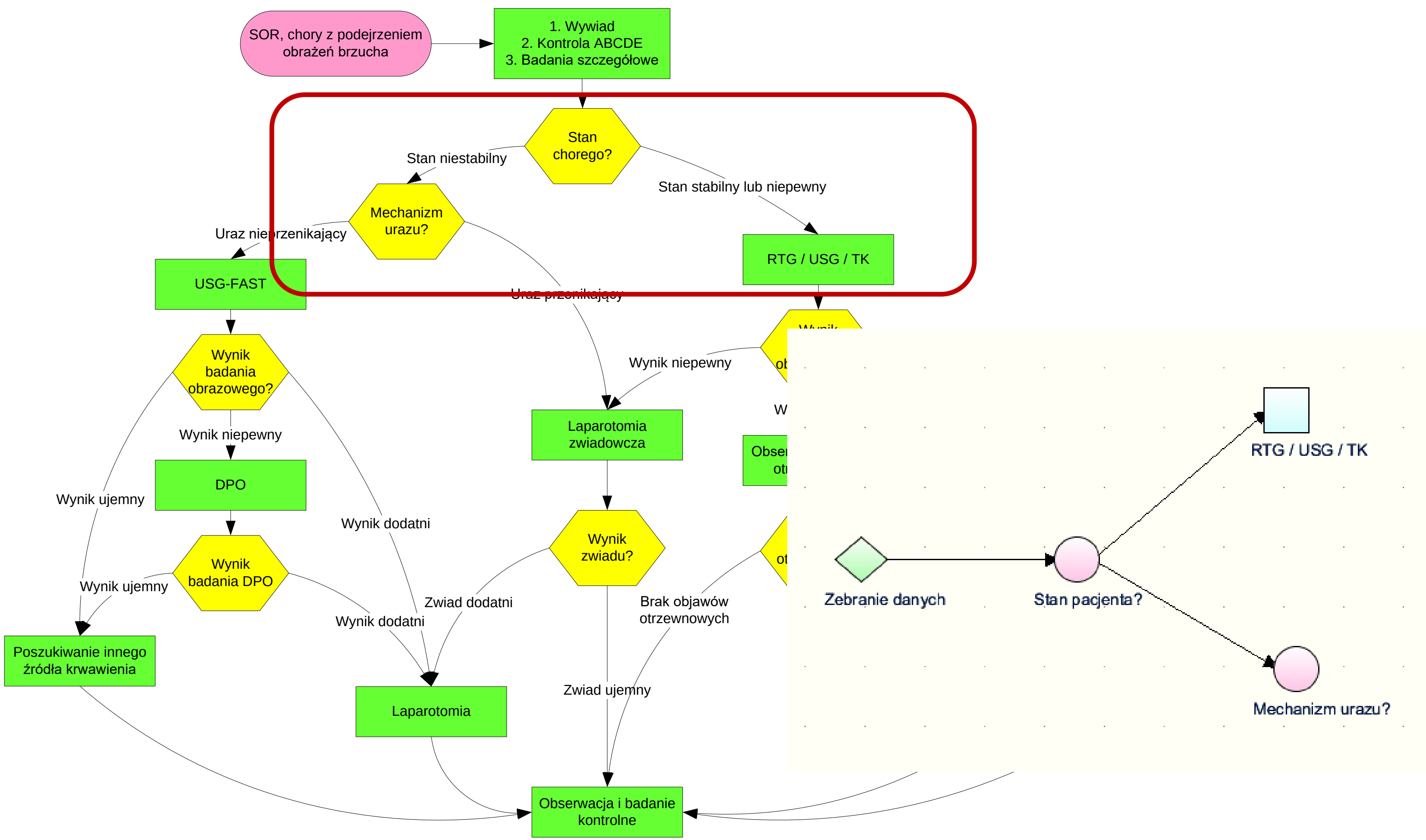
PROforma and OpenClinical.net

- PROforma
  - A scientific project (Cancer Research UK, 1992-now)
  - A commercial product Alium (Deontics, UK)

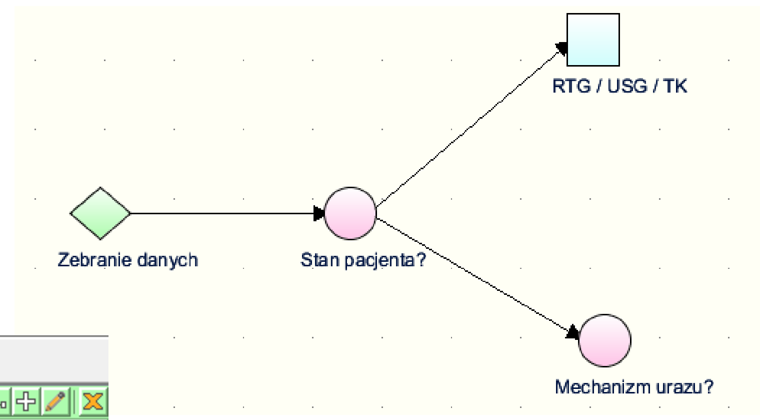
https://deontics.com/

- OpenClinical.net
  - Web-based repository of CIGs represented in PROforma
  - Peer-driven review and verification of submitted CIGs before they are made widely available
  - Possibility of running (simulating) available algorithms through a web-based system

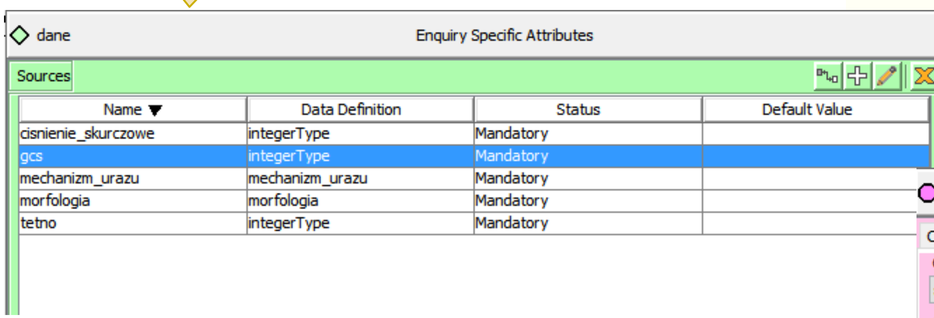
Example – CIG for abdomen trauma

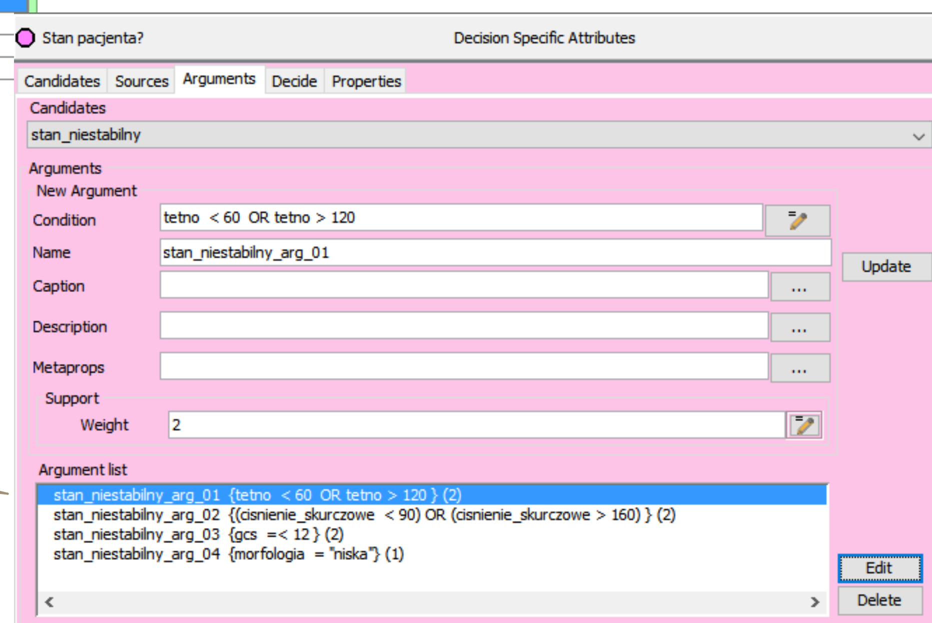


Definition of a decision step



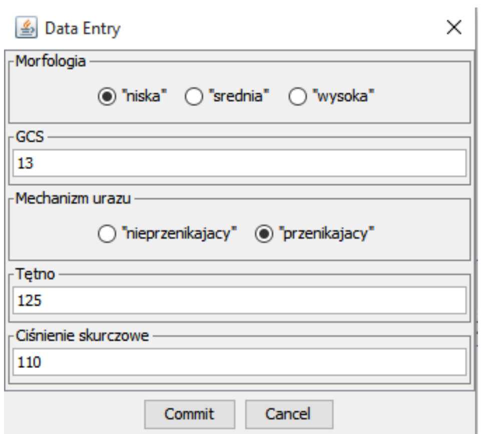
A detailed specification of data items to be colleted



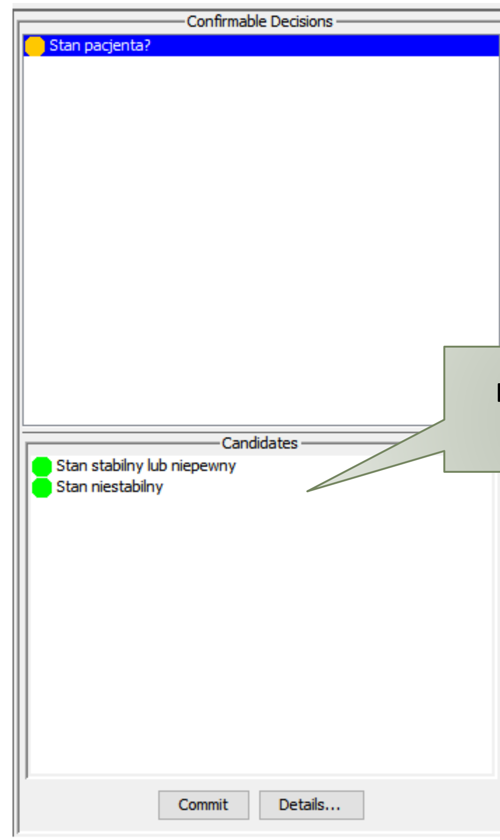


Specification of arguments **for** and **against** a specific decision option

Supervised decision making

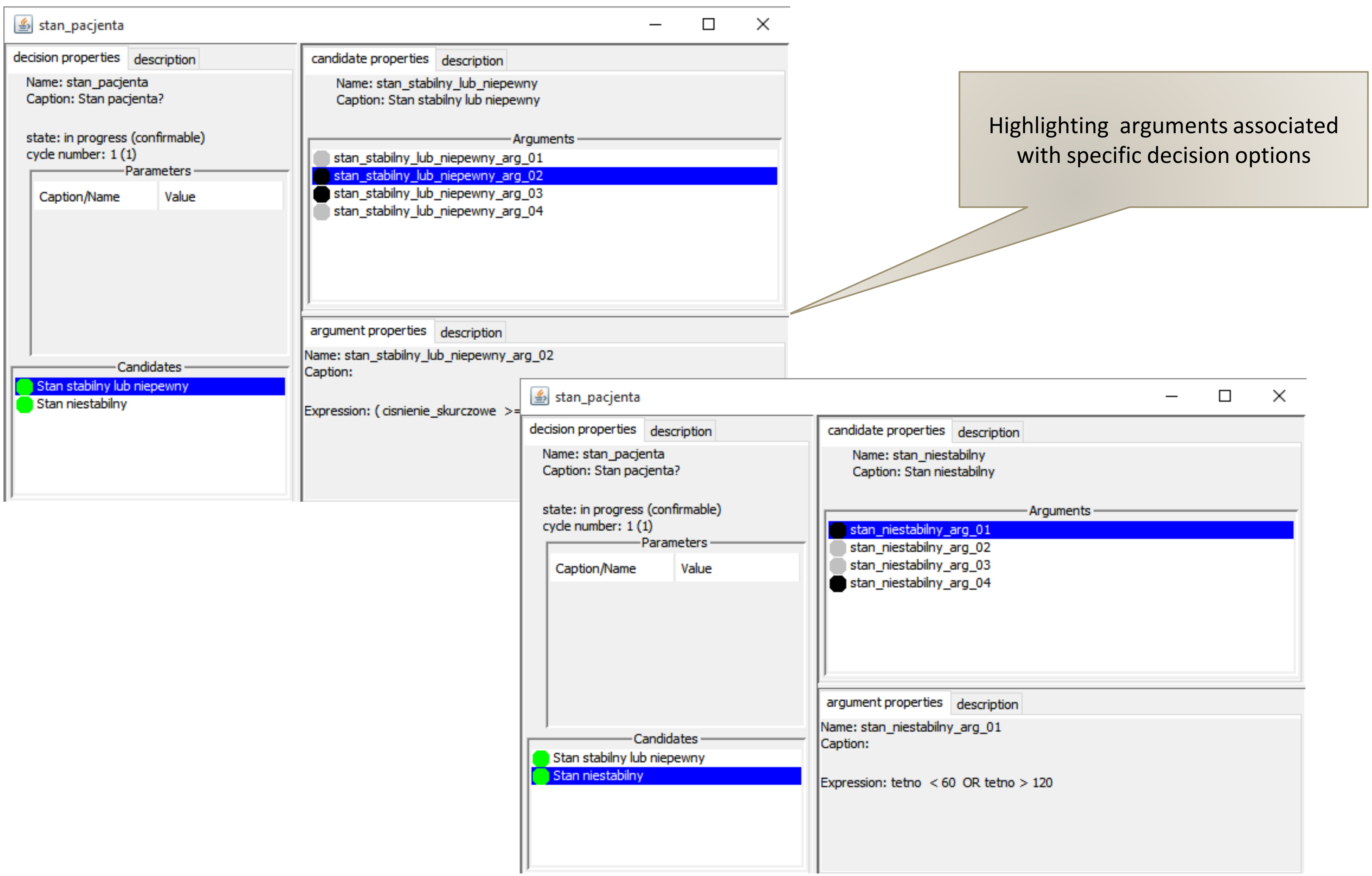


Provided patent data

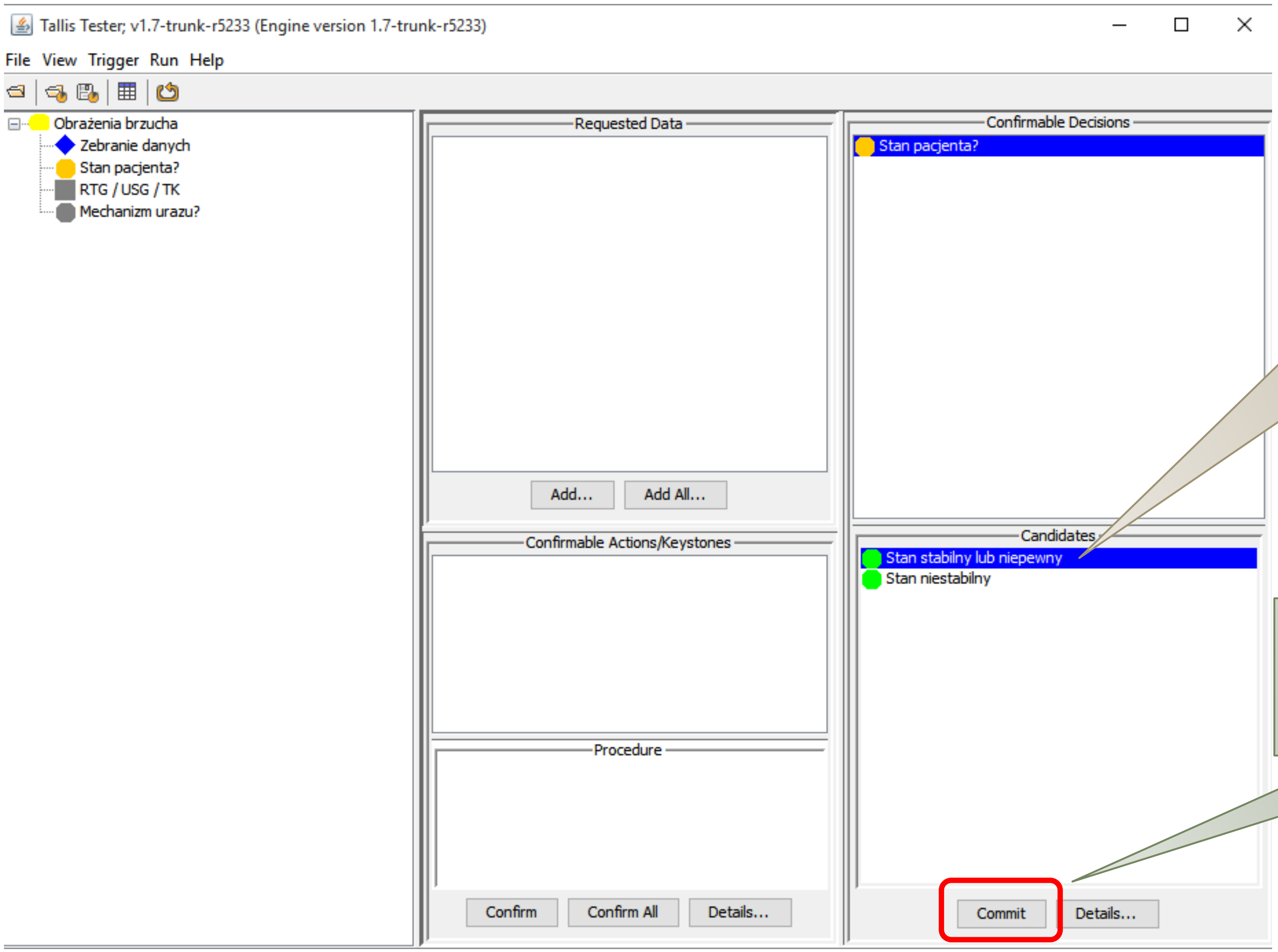


Both decision options are possible

Supervised decision making



Supervised decision making



If this option is selected, additional imaging procedures (defined in CIG) will be prescribed.

A physician may overwrite any option suggested by a system (and select one with “poor” support).

Patterns of collaboration

- Goal-based workflow representation based on PROforma
- State-based exceptions for detecting obstacles and hazards and associated plans for handling them
- Formal description of two collaboration patterns
  - *Assignment* → provider is accountable for outcome and responsible for handling exceptions
  - *Delegation* → client is responsible for outcome and responsible for managing (selected) exceptions

M.A. Grando, M. Peleg, M. Cuggia, D. Glasspool: Patterns for Collaborative Work in Health Care Teams. *Artificial Intelligence in Medicine*, 2011, 53 (3), 139-160.

Patterns of collaboration

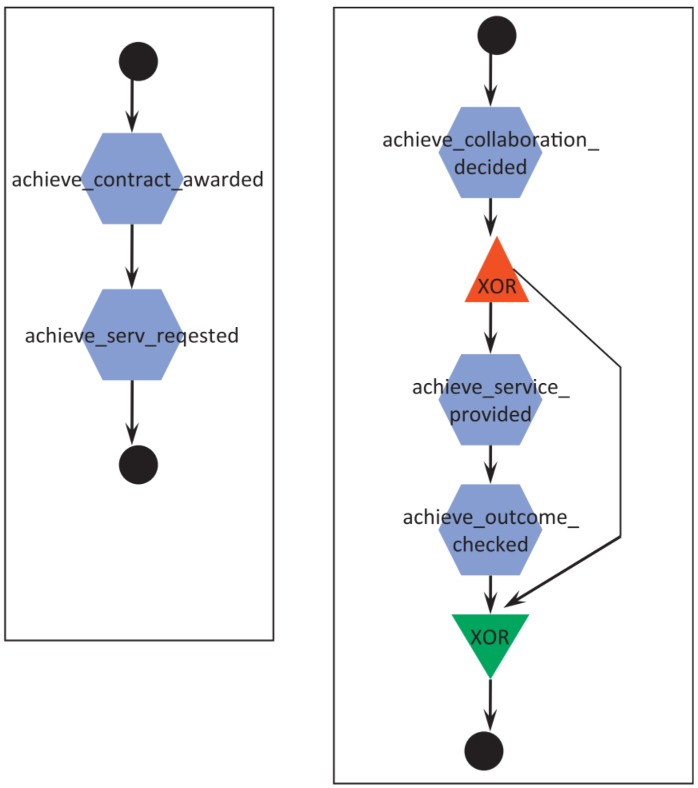


Fig. 2. (1) Client_assignment_pattern, (2) Provider_assignment_pattern. The hexagons represent goals, the triangles corresponds to split points and the inverted triangles to join points.

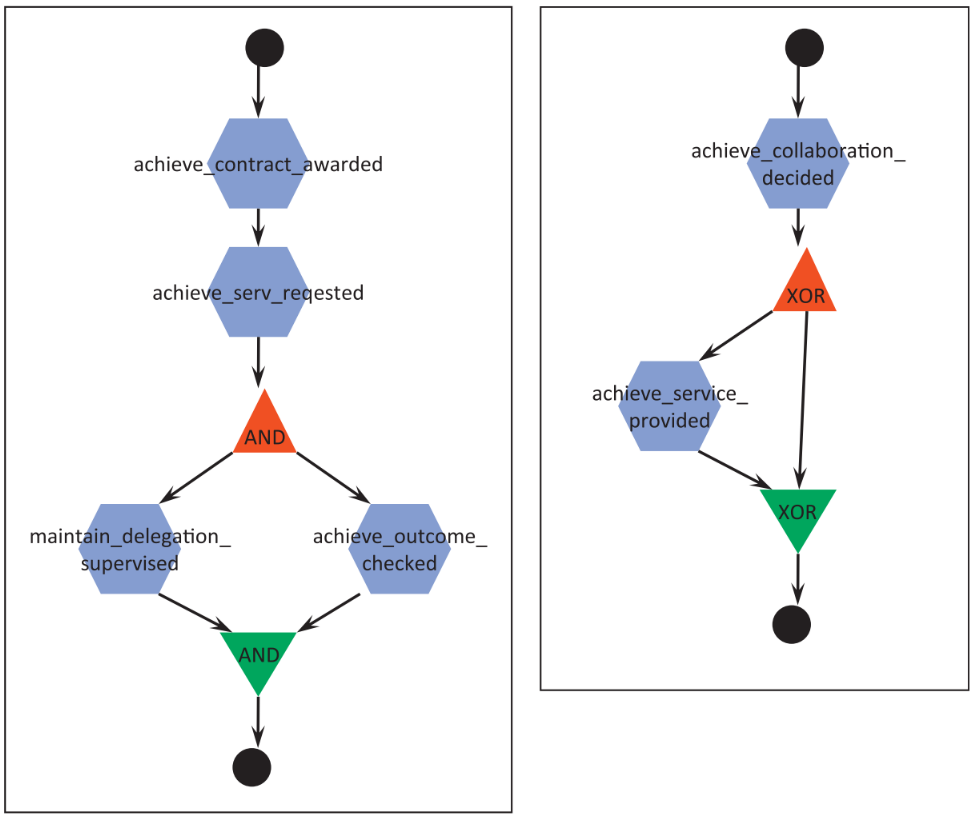
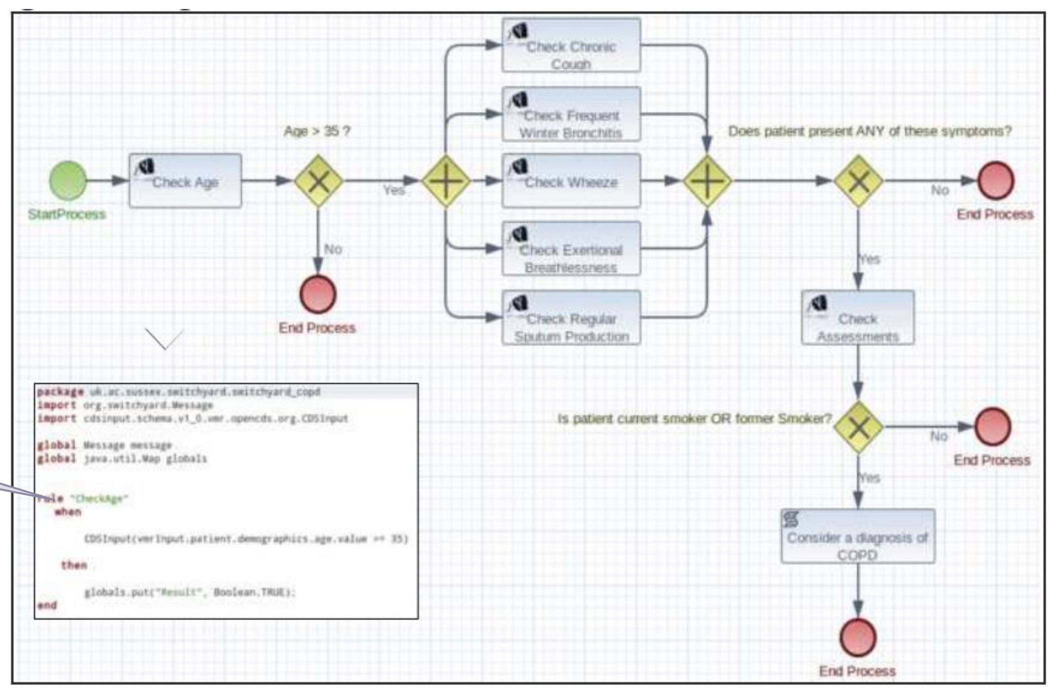


Fig. 6. (1) Client_delegation_pattern and (2) Provider_delegation_pattern.

CIGs in BPMN

- Combination of BMPN (jBPM) and rules (Drools) to represent a CIG, integration with HIS via SOA

Decision rules associated with specific tasks to establish decision outcomes



Rodriguez-Loya, S., Aziz, A., & Chatwin, C. (2014). A Service Oriented Approach for Guidelines-based Clinical Decision Support using BPMN. *Studies in Health Technology and Informatics*, *205*, 43–47.

SUPPORT FOR MULTI-MORBIDITIES

Practical motivation

- 76% of people 65+ years old have 2+ chronic conditions, and their care costs are 5.5 times higher than for non multi-morbid patients [Bähler, et al. 2015]
- Direct application of multiple CPGs "*may have undesirable effects*" and "*diminish the quality of care*" [Boyd et al. 2005]
- No support for multi-morbid conditions is a "*major shortcoming of CPG uptake in clinical practice*" [Peleg, 2013]

Methodological challenge

One of the "grand challenges" for clinical decision support

"The challenge … to identify and eliminate redundant, contraindicated, potentially discordant, or mutually exclusive guideline based recommendations for patients presenting with comorbid conditions or multiple medications." [Sittig et al., 2008]

A new, "*combinatorial, logical, or semantic*" methodological approach is needed [Fox et al. 2010]

LOGIC-BASED CIG PERSONALIZATION FRAMEWORK

Research goal and questions

Goal: a framework for personalizing CPGs for multi-morbid patients by
(1) **mitigating** adverse interactions and
(2) **customizing** resulting therapies based on patients' **preferences**

1. How to represent rich primary (CPGs) and secondary (interactions, preferences) clinical knowledge?
2. What "reasoning" techniques to use to process knowledge encoded in the proposed formalism?

Answer: first-order logic,
theorem proving and model solving

Wilk, S., Michalowski, M., Michalowski, W., Rosu, D., Carrier, M., & Kezadri-Hamiaz, M. (2017). Comprehensive mitigation framework for concurrent application of multiple clinical practice guidelines. *Journal of Biomedical Informatics*, *66*.

Patient preferences

- A new and important component of EBM

EBM = Evidence + Experience + Preferences

"evidence is never enough to make treatment recommendations" [Murad et al., 2008]

- Preferences are especially relevant when evidence is associated with a high level of uncertainty (→ "grey zone" or "preference-sensitive" decisions) [van der Weijden et al., 2013]
- Participation of patient groups already in the development of CPGs [van der Weijden et al., 2010]

First-order logic (FOL)

- A formal system to represent and reason about knowledge
- Knowledge represented using a domain-specific language with **logical** (fixed meaning) and **non-logical** symbols

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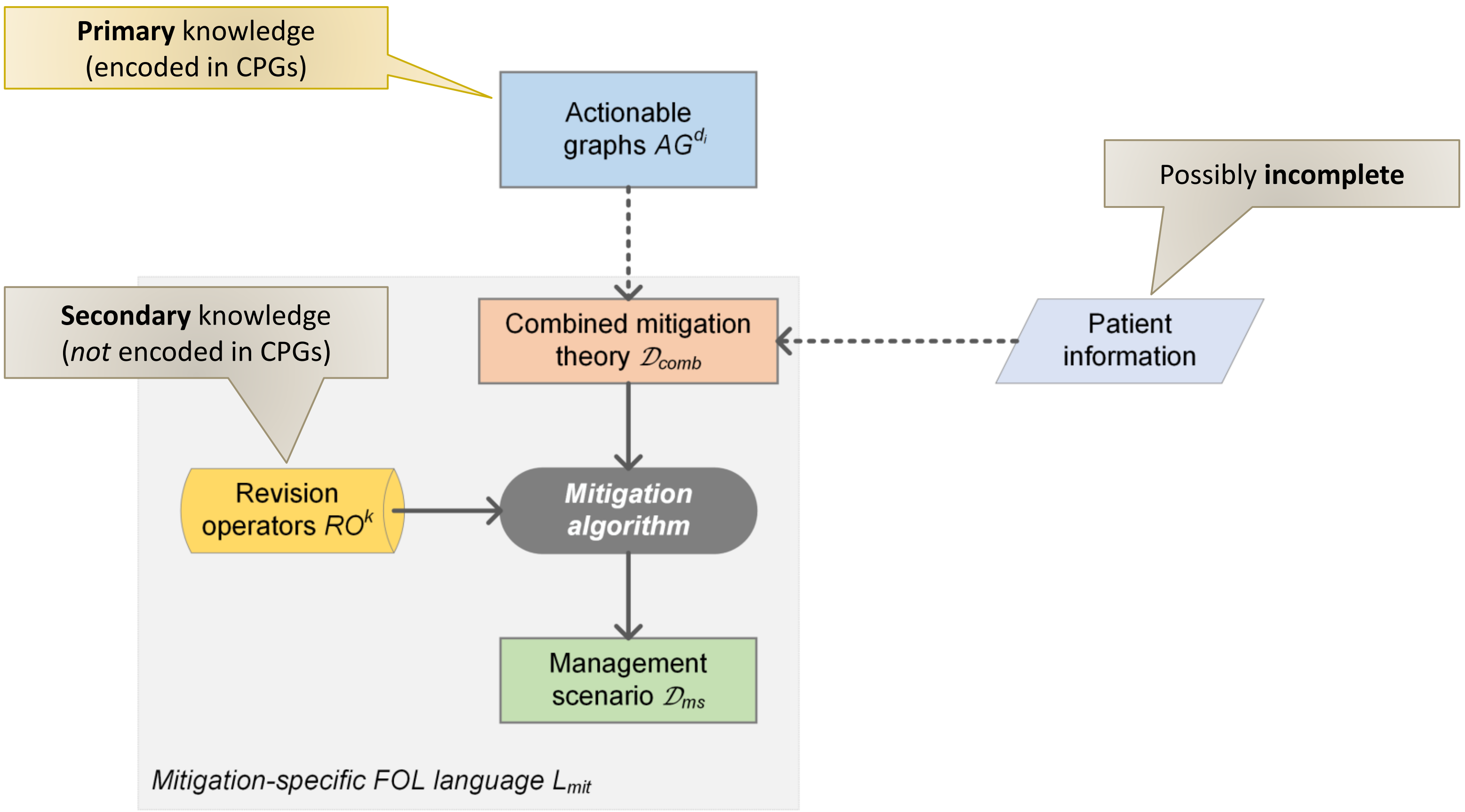
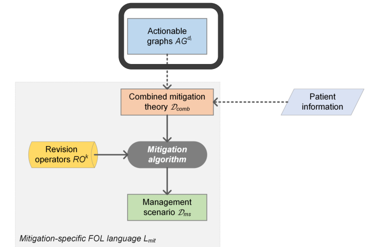
- A **theory** $\mathcal{D}$ is a collection of sentences
- An **interpretation** $\mathcal{I}$ assigns the meaning (formal semantics) to non-logical symbols
- If $\mathcal{I}$ satisfies all sentences in $\mathcal{D}$, then it is called a **model** for $\mathcal{D}$

- **Theorem proving** ($\rightarrow$ checking for consistency and entailment) and **model finding** techniques

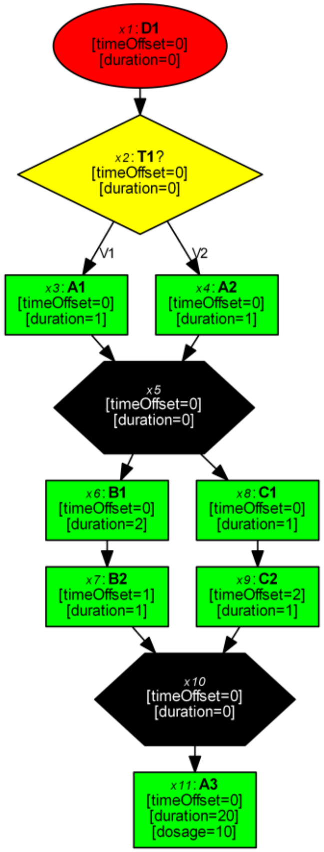
FOL-based personalization framework



Actionable graph AG^{d_i}



- Captures a CPG for a given disease d_i
- An intermediate representation based on a task-network model for better interoperability
- Can be automatically obtained from other representations (e.g. GLIF3, SAGE)
- A directed graph with context, decision, action and parallel nodes (with additional attributes)



Mitigation-specific language L_{mit}

- Allows describing all components of the mitigation problem
- Introduces **structural** and **temporal** predicates

Table 1: Structural predicates in L_{mit} (d, t, a and v are labels identifying a specific disease, decision, action, and result respectively, dosage is given in logical units)

Predicate	Description
$node\,(x)$	
$disease(x$	
$decision($	
$action(x,$	
$parallel(x$	
$directPre$	
$prec\,(x, y)$	
$dosage(x,$	
$result(x,$	

Table 2: Temporal predicates in L_{mit} (times and durations are given in logical units, execution period of an activity associated with a node x is determined by its starting time and duration)

Predicate	Description
$timeOffset(x, to)$	node x occurs to time units after the preceding node
$duration(x, dt)$	node x takes dt time units to complete
$startTime(x, st)$	node x starts at time st
$currentTime\,(ct)$	current patient time is ct
$happensNowOrLater\,(x)$	activity (decision or action) from node x is happening now (given current time) or will happen in future
$overlap\,(x, y)$	execution periods of nodes x and y overlap
$overlapNowOrLater\,(x, y)$	execution periods of nodes x and y are overlapping now (given current time) or will overlap in the future

Combined mitigation theory $\mathcal{D}_{comb}$

- Captures core components of a mitigation problem
- Defined as a triple $\langle \mathcal{D}_{common}, \mathcal{D}_{cpg}, \mathcal{D}_{pi} \rangle$, where
  - $\mathcal{D}_{common}$ – common axioms defining universal character of CPGs, e.g.,

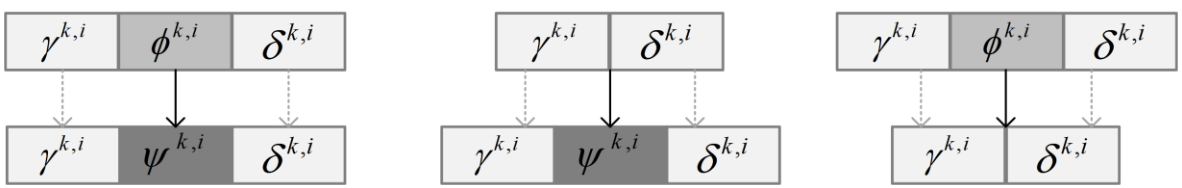
1. $\forall x, stx, dtx : node(x) \wedge startTime(x, stx) \wedge duration(x, dtx) \implies endTime(x, stx + dtx)$
2. $\forall x, etx, ct : node(x) \wedge endTime(x, etx) \wedge currentTime(ct) \wedge (ct < etx) \implies happensNowOrLater(x)$

  - $\mathcal{D}_{cpg}$ – a union of theories $\left(\mathcal{D}_{cpg}^{d_1} \cup \mathcal{D}_{cpg}^{d_2} \cup \cdots \cup \mathcal{D}_{cpg}^{d_k}\right)$ representing AGs applied to a comorbid patient
  - $\mathcal{D}_{pi}$ – a collection of available patient data (results of tests and examinations, prescribed therapies, …)

Revision operator RO^k

- Defines revisions to CPGs ($\mathcal{D}_{cpg}$) triggered by some undesired circumstances (related to **preferences** or **interactions**)
- Defined as a pair $\langle \alpha^k, Op^k \rangle$, where
  - α^k – undesired circumstances that need to be addressed
  - Op^k – a list of operations that revise $\mathcal{D}_{cpg}$ (**only**) to address α^k
- Each $Op^{k,i}$ from Op^k defines a single *find-and-replace* operation ($\longrightarrow$ replace, insert, delete)

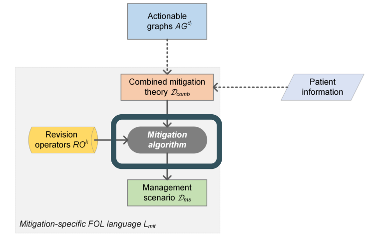
$Op^{k,i} = \langle \gamma^{k,i}, \phi^{k,i}, \delta^{k,i}, \psi^{k,i} \rangle$ $\quad$ $Op^{k,i} = \langle \gamma^{k,i}, \varepsilon, \delta^{k,i}, \psi^{k,i} \rangle$ $\quad$ $Op^{k,i} = \langle \gamma^{k,i}, \phi^{k,i}, \delta^{k,i}, \varepsilon \rangle$



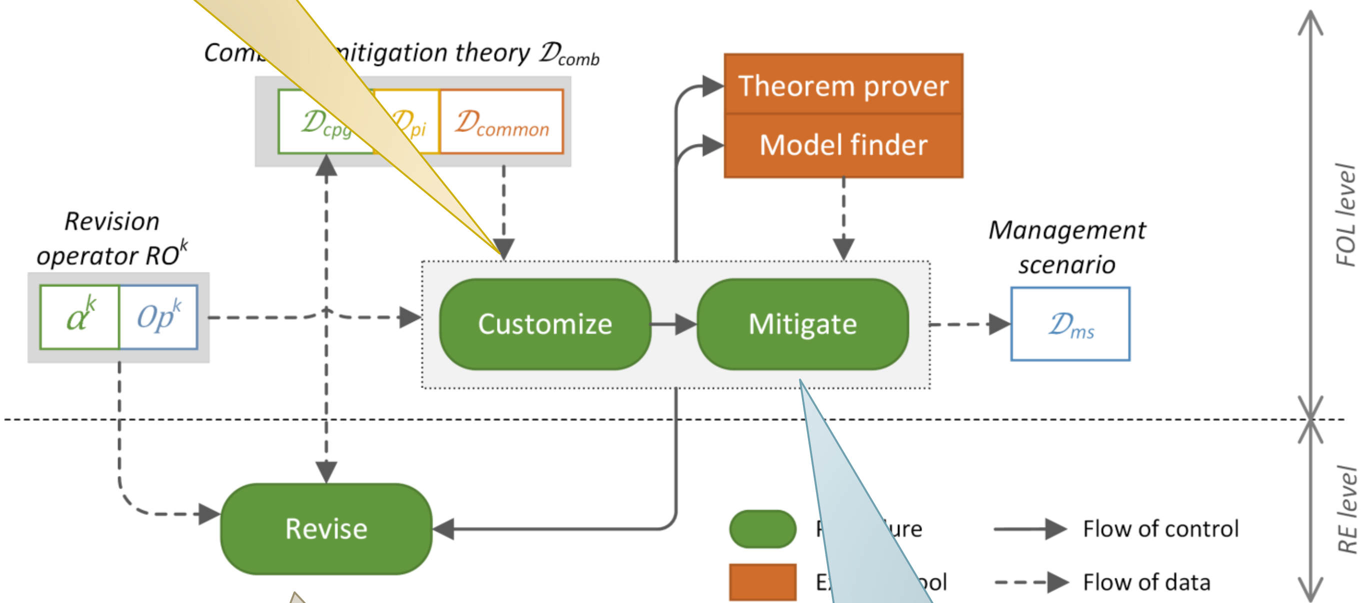
Management scenario $\mathcal{D}_{ms}$

- Represents a **safe** (no interactions) and **preferred** (consistent with preferences) course of actions for a given patient
- Specifies clinical actions to be taken with their order and timing
- Introduces assumptions related to the future patient's state

Mitigation Algorithm



Revises $\mathcal{D}_{cpg}$ to account for patient preferences

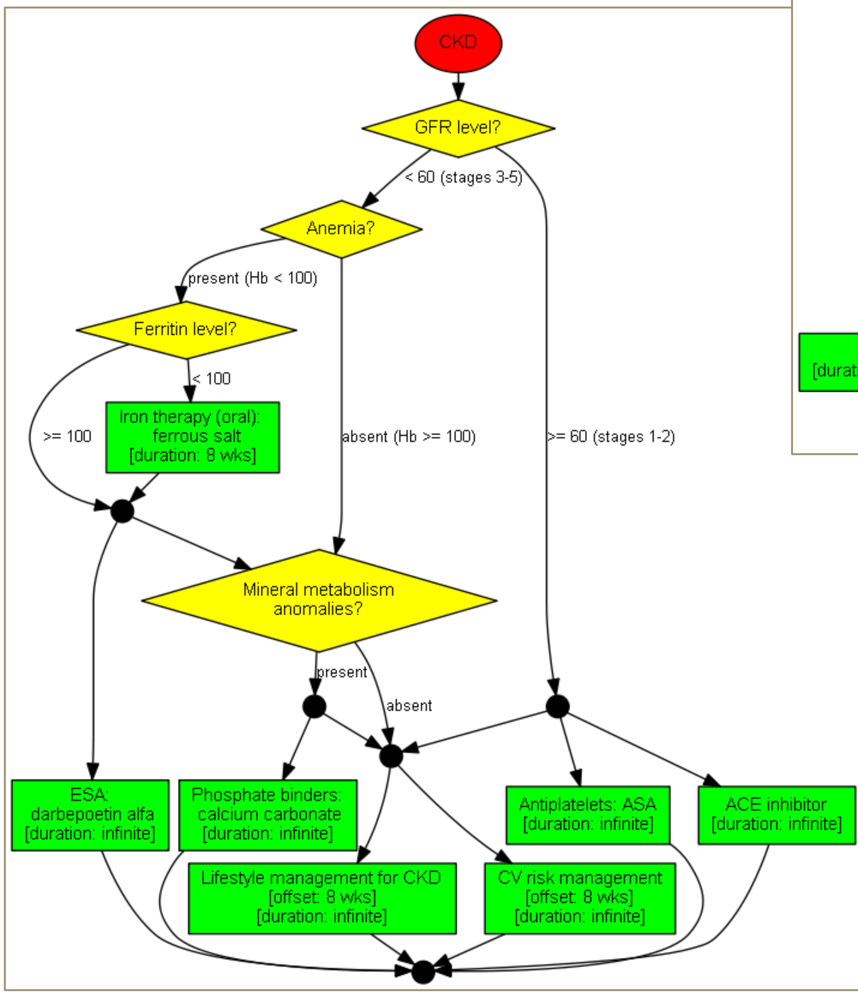


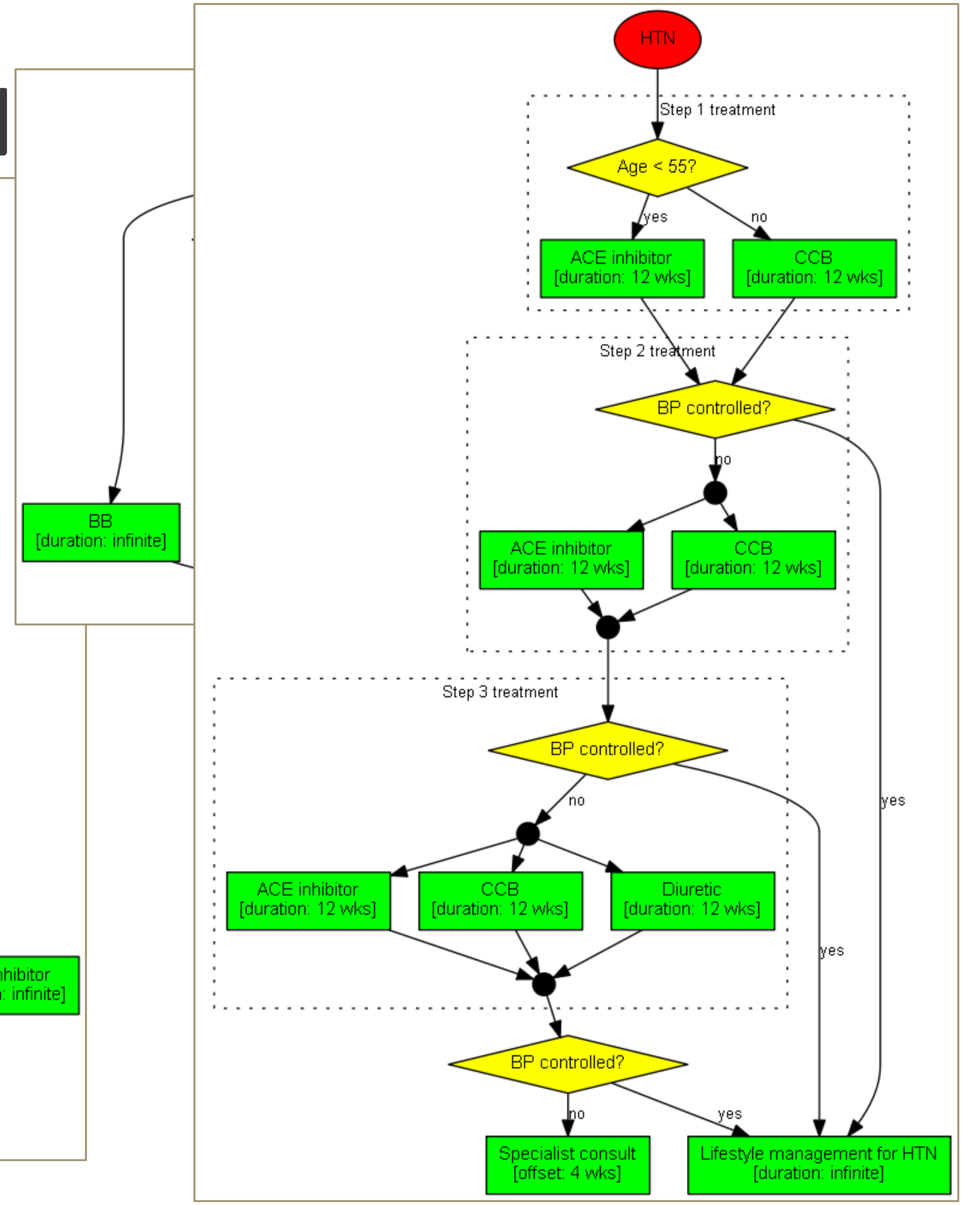
Revises $\mathcal{D}_{cpg}$ according to the currently applied RO^k

Revises $\mathcal{D}_{cpg}$ to avoid interactions and establishes $\mathcal{D}_{ms}$ (depth-first search)

Regular expression (RE) level

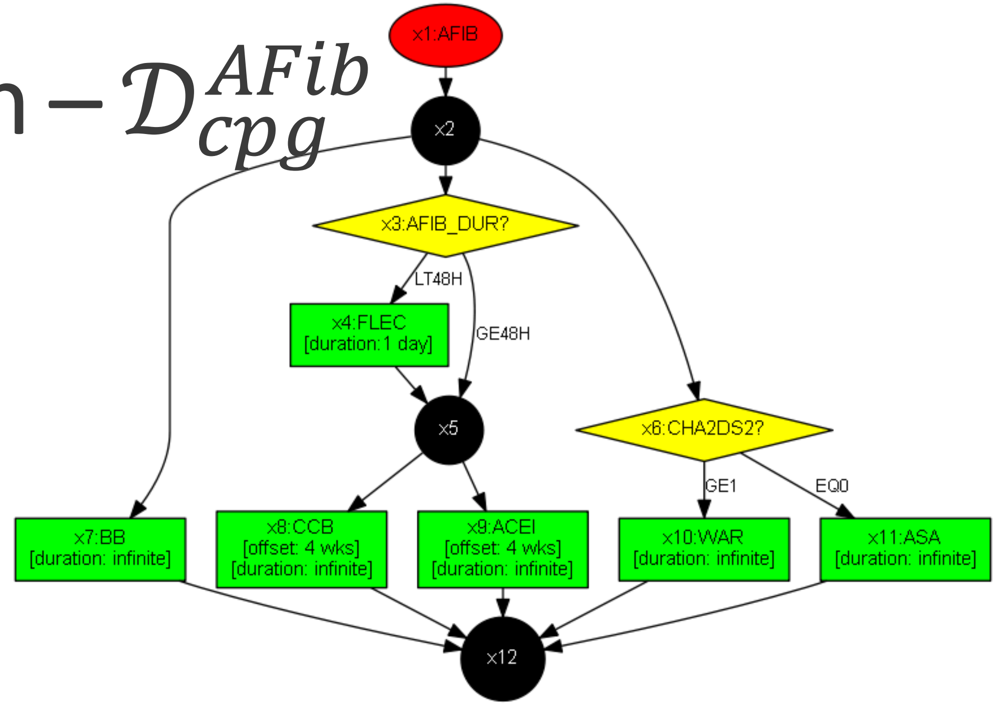
CKD, AFib and HTN





CKD = chronic kidney disease, AFib = atrial fibrillation, HTN = hypertension

FOL representation – $\mathcal{D}_{cpg}^{AFib}$



Simplified representation for brevity
(e.g. no *directPrec*)

```
exists x1,x2,x3,x4,x5,x6,x7,x8,x9,x10,x11,x12:
(disease(x1,AFIB) /\ parallel(x2) /\ action(x7,BB) /\ parallel(x12)) /\
(((disease(x1,AFIB) /\ parallel(x2) /\ decision(x3,AFIB_DUR) /\ result(x3,LT48H) /\ action(x4,FLEC)
          /\ parallel(x5) /\ action(x8,CCB) /\ parallel(x12)) /\
  (disease(x1,AFIB) /\ parallel(x2) /\ decision(x3,AFIB_DUR) /\ result(x3,LT48H) /\ action(x4,FLEC)
          /\ parallel(x5) /\ action(x9,ACEI) /\ parallel(x12))) \/
 ((disease(x1,AFIB) /\ parallel(x2) /\ decision(x3,AFIB_DUR) /\ result(x3,GE48H)
          /\ parallel(x5) /\ action(x8,CCB) /\ parallel(x12)) /\
  (disease(x1,AFIB) /\ parallel(x2) /\ decision(x3,AFIB_DUR) /\ result(x3,GE48H)
          /\ parallel(x5) /\ action(x9,ACEI) /\ parallel(x12)))) /\
((disease(x1,AFIB) /\ parallel(x2) /\ decision(x6,CHA2DS2) /\ result(x6,GE1)
          /\ action(x10,WAR) /\ parallel(x12)) \/
 (disease(x1,AFIB) /\ parallel(x2) /\ decision(x6,CHA2DS2) /\ result(x6,EQ0)
          /\ action(x11,ASA) /\ parallel(x12)))
```

Interaction-Related Revision Operators

- RO^1_{int}: if patient diagnosed with HTN and CKD, then remove

$$RO^2_{int} = < \alpha^2, \{Op^{2,1}\} >$$

$$\alpha^2 = \exists x1, x2, x3, x4 :$$

$$disease\,(x1, HTN) \wedge disease(x2, CKD) \wedge disease\,(x3, AFib) \wedge action\,(x4, DIUR) \wedge happensNowOrLater\,(x4)$$

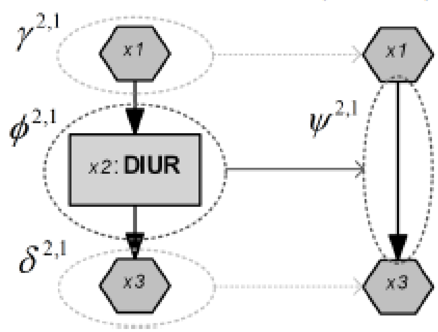
$$Op^{2,1} = \langle \gamma^{2,1}, \phi^{2,1}, \delta^{2,1}, \psi^{2,1} \rangle$$

$$\gamma^{2,1} = parallel\,(x1)$$

$$\phi^{2,1} = directPrec\,(x1, x2) \wedge action\,(x2, DIUR) \wedge directPrec\,(x2, x3)$$

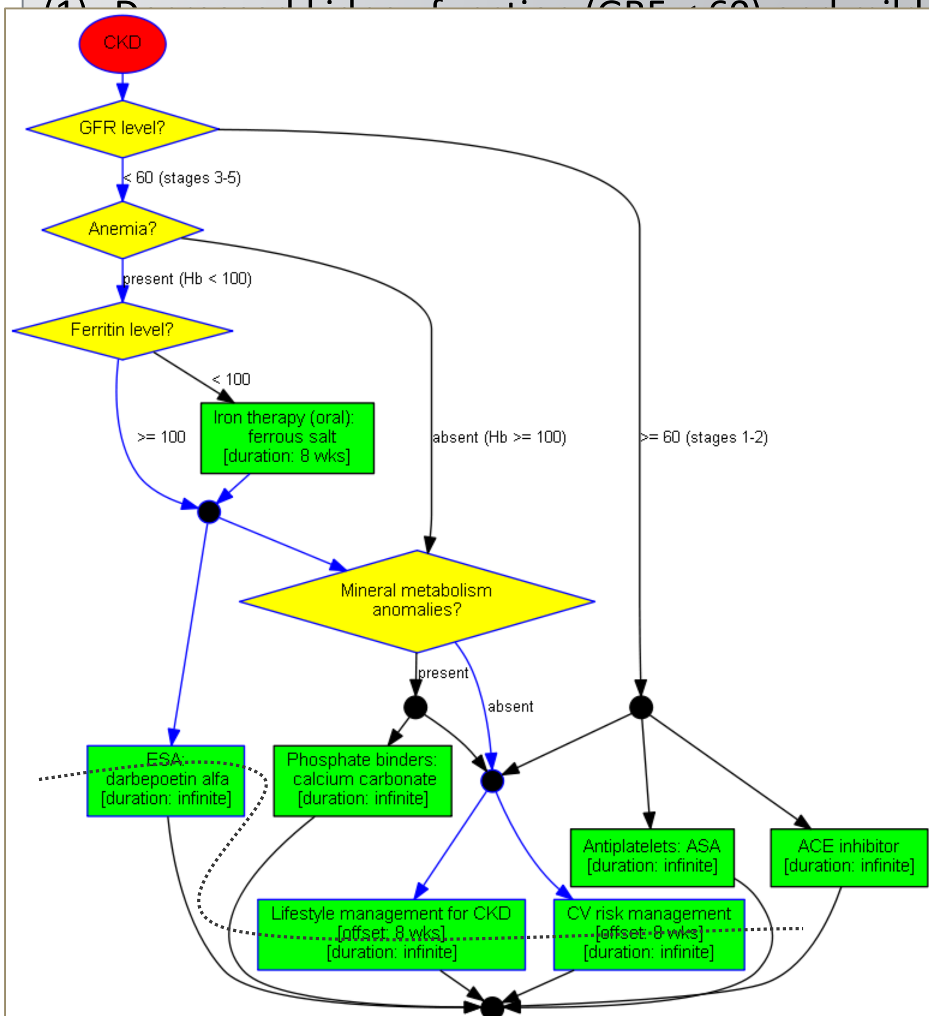
$$\delta^{2,1} = parallel\,(x3)$$

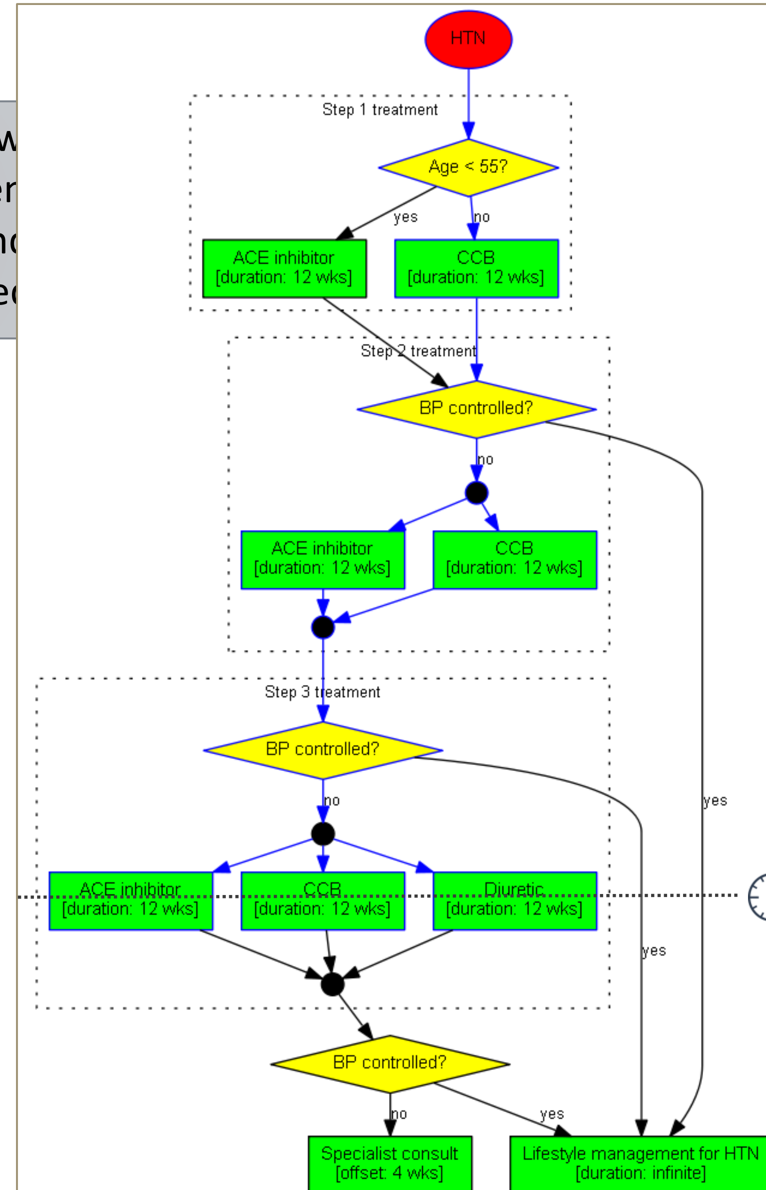
$$\psi^{2,1} = directPrec\,(x1, x3)$$



Patient scenario

A 70-years old male with CKD and HTN having the follow





Patient scenario

For the last 12 hours patient has been experiencing irregular pulse, breathlessness, dizziness, and chest discomfort. Upon admission to the ED patient has been diagnosed with AFib that has been confirmed by standard ECG recording. Patient's CHA_2DS_2 score is 2.

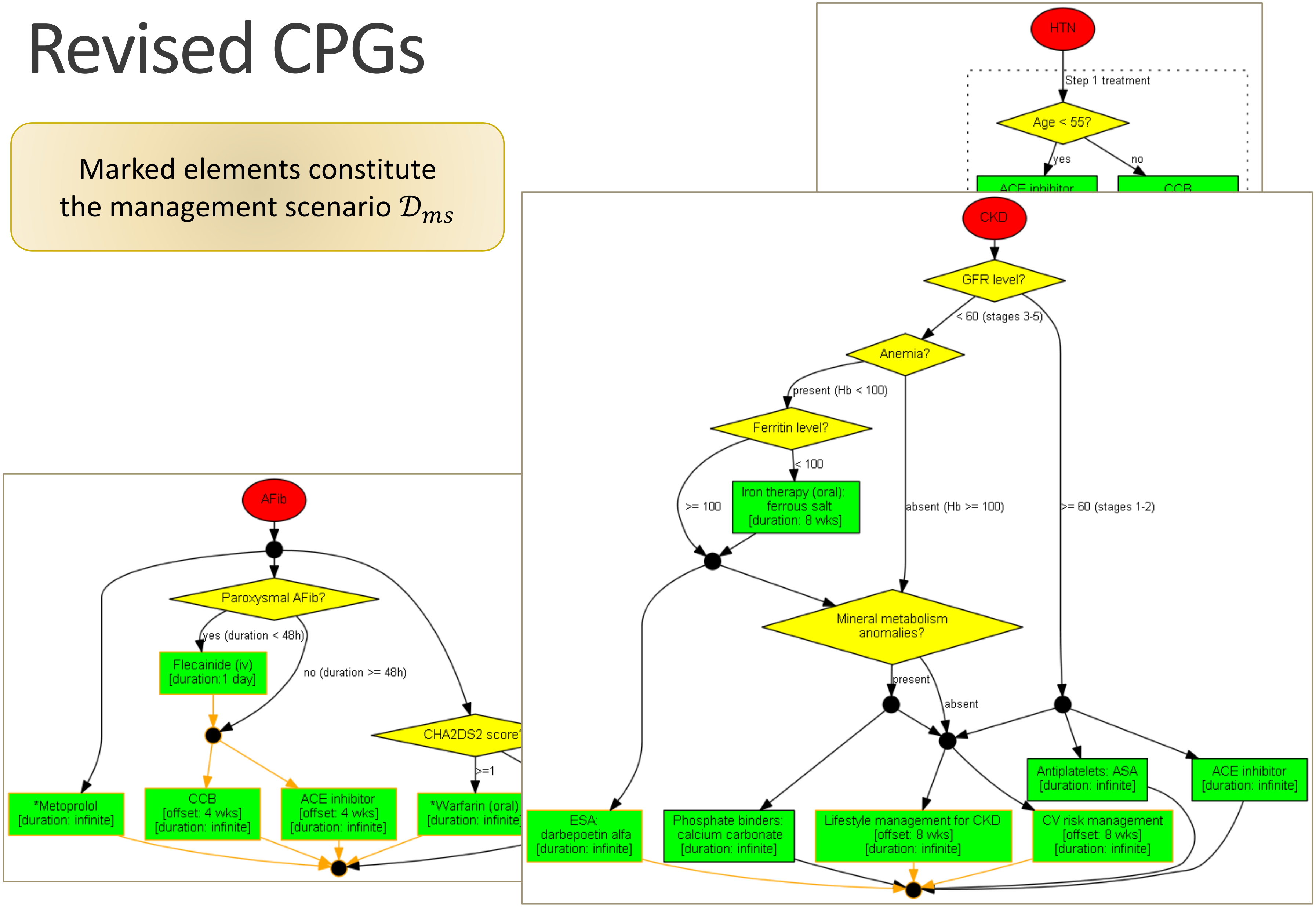
Patient has expressed preferences related to AFib therapy:
RO^1_{pref}: if diagnosed with AFib and prescribed warfarin, then replace warfarin with apixaban (one of the DOACs)

Personalization framework is invoked

1. `customize` procedure applies RO^1_{pref} and revises CPG for AFib
2. `mitigate` procedure checks applicable RO^k_{int}
   - RO^1_{int} → changes affect past actions (step 1 in CPG for HTN) and thus they are not introduced by `revise` procedure
   - RO^2_{int} → diuretics are removed from CPG for HTN
   - RO^3_{int} → apixaban is discarded and warfarin is restored in CPG for AFib
   - RO^4_{int} → BB in replaced by metoprolol in CPG for AFib

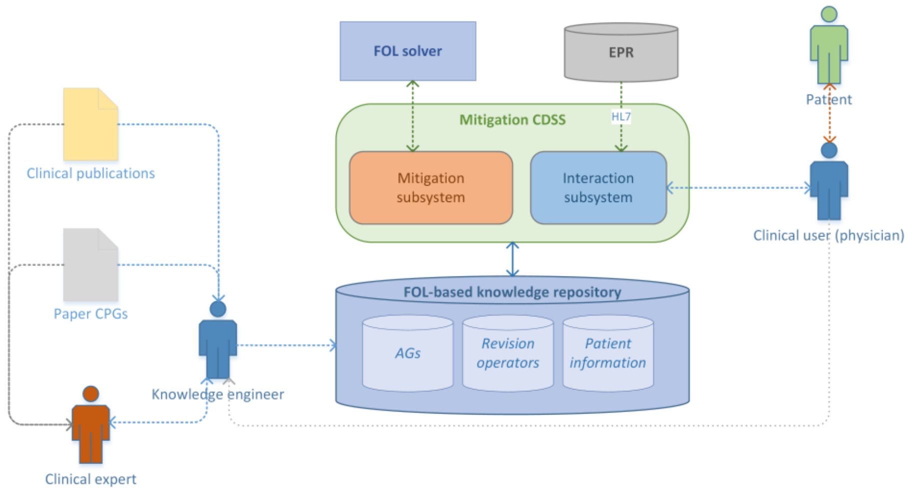
Revised CPGs

Marked elements constitute the management scenario $\mathcal{D}_{ms}$



Implementation and extension

- Complex FOL-based representation of primary and secondary knowledge, but hidden from clinicians



- Transforming the reasoning problem into planning one expressed in the Planning Domain Definition Language (PDDL)

GOAL-BASED MITIGATION FRAMEWORK

Goal-based mitigation framework

- Employs knowledge in National Drug File – Reference Terminology (NDF-RT) with information about prevention, treatment and physiological effects
- Relies on PROforma, however, CIGs are represented as high-level plans associated with goals with statements from NDF-RT
- Use of SNOMED-CT to encode information and HL7 FHIR to exchange information between PROforma engine and HIS
- **Controller** component oversees all events associated with CIG enactment, identifies conflicts and interact with a physician to solve these conflicts

Kogan, A., Tu, S. W., & Peleg, M. (2018). Goal-driven management of interacting clinical guidelines for multimorbidity patients. *AMIA ... Annual Symposium Proceedings. AMIA Symposium*, *2018*(October), 690–699.

NDF-RT

- owl:Thing
  - **'Cellular or Molecular Interactions [MoA]'**
  - **'Chemical Ingredients [Chemical/Ingredient]'**
  - **'Clinical Kinetics [PK]'**
  - DIRECTED-BINARY-RELATION
  - **'Diseases, Manifestations or Physiologic States [Disease/Finding]'**
  - **'Dose Forms [Dose Form]'**
  - PAL-CONSTRAINT
  - **'Pharmaceutical Preparations'**
  - **'Physiological Effects [PE]'**
  - **'Therapeutic Categories [TC]'**
  - **'VA Drug Interactions [VA Drug Interaction]'**

ASPIRIN

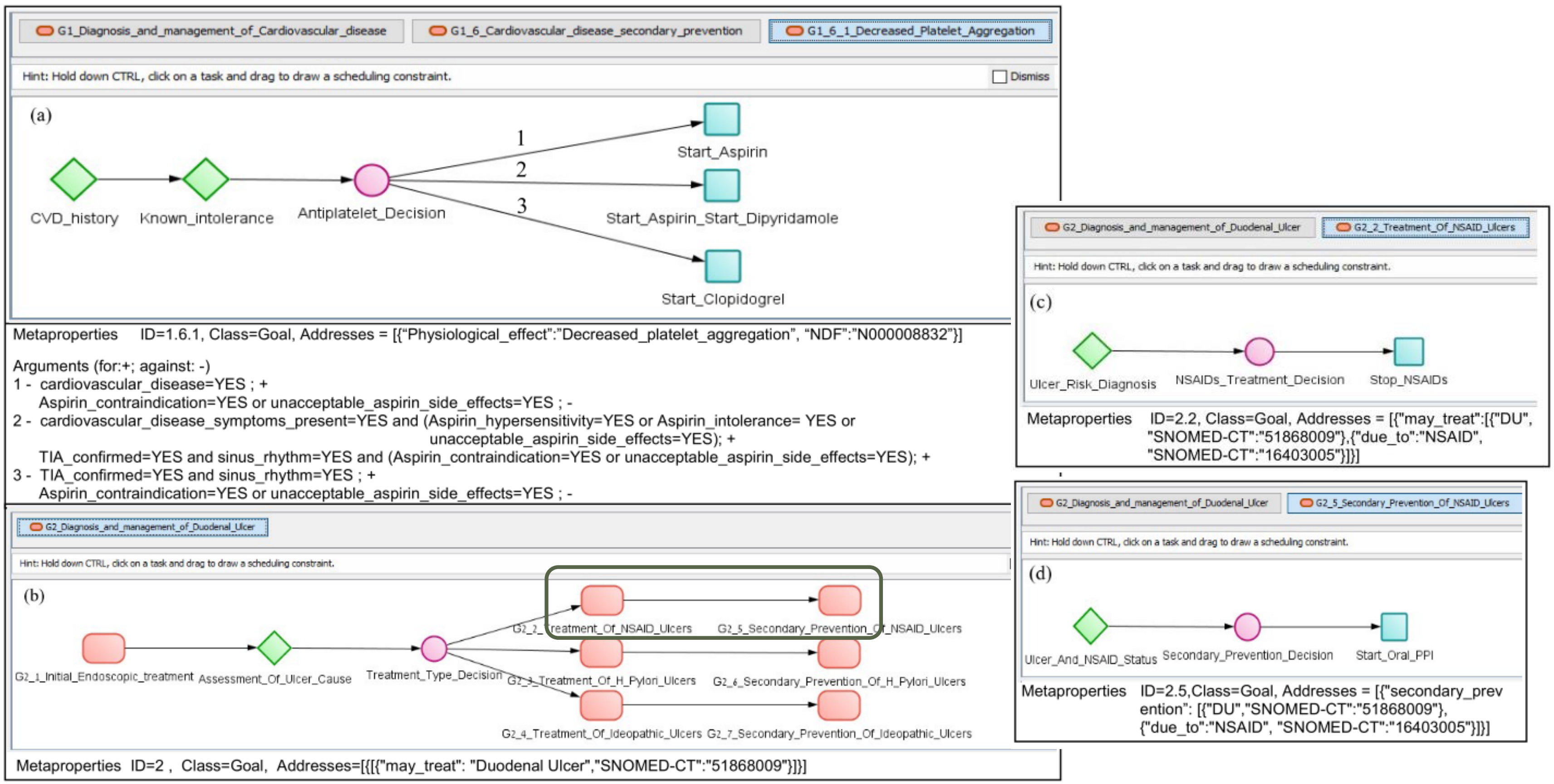
DU is-a Hemorrhagic Disorder

Physiological Effect fulfills the abstract goal "prevent blood clots"

CI_with some 'Hemorrhagic Disorders [Disease/Finding]'	has_PE some 'Decreased Platelet Activating Factor Production [PE]'
CI_with some 'Infant [Disease/Finding]'	has_PE some 'Decreased Platelet Aggregation [PE]'
CI_with some 'Nasal Polyps [Disease/Finding]'	has_PE some 'Decreased Prostaglandin Production [PE]'
CI_with some 'Pregnancy Third Trimester [Disease/Finding]'	has_PE some 'Decreased Thromboxane Production [PE]'

Patient Scenario

A patient who had cardiovascular disease (CVD) and, following the CIG's recommendations for secondary prevention of CVD via decreased platelet aggregation, was started on aspirin. The patient developed duodenal ulcer (DU).



Goal forest

Controller retrieves from PROfoma and controls a current goal forest

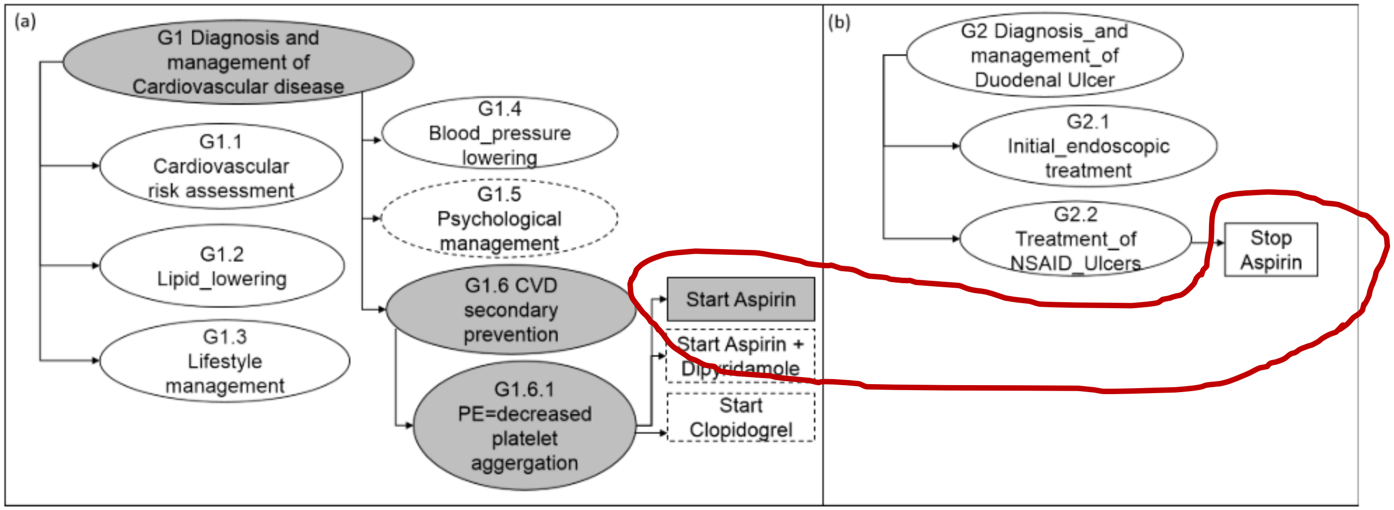


Figure 3. The patient's goal forest as retrieved by the Controller from the CVD and DU guidelines. CIG plans are represented as goals and depicted as ellipses. CIG actions are the leaves, depicted as rectangles. The goal trees are hierarchical and contain all the goals that were inferred by the PROforma engine for the specific patient as the CIGs were traversed (in DU till G2.2), they do not contain goals that were not deemed relevant for the patient, shown with dotted lines. Goals that are not satisfied are shown in grey. (a) The CVD goal tree is unsatisfied due to the inconsistency between goals G1.6.1 and G2.2. Since G1.6.1 is unsatisfied its parents are also unsatisfied. (b) The DU goal tree that has been acquired till Goal G2.2.

Controller rules

Rules for controlling the forest, indicating conflicts and solving them (by interacting with the user)

α = Goal_Forest(?goal_forest) and Is_Member_Of(?goal1, ?goal_forest) and Is_Member_Of(?goal2, ?goal_forest);
β = α and Log(?log) and (?action1.type=medication) and (?action2.type=medication) and Has_Medication_Request_Order(?action1) and Has_Medication_Request_Proposal(?action2) and Has_Action(?goal1,?action1) and Has_Action(?goal2,?action2);

a. //Pass data and run CIG
If (Patient_Thread (?patient_thread) and Problem (?diagnosis) and Has_Guideline (?diagnosis, ?guideline))
⇒ Insert_PROforma_Data(?patient_thread, ?guideline),
⇒ Run_PROforma_Guideline(?guideline),
⇒ ?guideline.status ← 'active',
⇒ ?guideline.state ← 'build goal tree'

b. //Build goal tree and add to forest
If (Guideline(?guideline) and (?guideline.state = 'build goal tree') and Goal_Forest(?goal_forest) and Log(?log))
⇒ ?API_Tasks ← Retrieve_Tasks(?guideline),
⇒ ?goal_tree ← Initiate_Goal_Tree(?API_Tasks),
⇒ Add_Tree_To_Forest (?goal_tree, ?goal_forest),
⇒ ?goal_tree.status ← 'active',
⇒ ?guideline.state ← 'goal_tree_built'

c. //Detect inconsistent Physiological Effect (PE) goals
If (α and Is_Equal(?goal1.object,?goal2.object) and Is_Inconsistent(?goal1.PE_verb, ?goal2.PE_verb))
⇒ Flag_Verb_Inconsistent_Goals(?goal1, ?goal2, ?log),
⇒ Assert(Is_Verb_Inconsistent(?goal_forest))

d. //Detect inconsistent actions
If (β and Is_Equal_or_subsumed (?action1.object,?action2.object) and Is_ Inconsistent (?action1.verb, ?action2.verb))
⇒ Flag_Action_Inconsistent(?action1,?goal1, ?action2, ?goal2, ?log)

e. //Get user preference regarding conflicting actions
If (β and Is_Action_Inconsistent(?action1,?goal1, ?action2, ?goal2, ?log))
⇒ If (User_Preference(?goal2, 'cancel')) then ?goal2.status ← 'cancel'
else if User_Preference(?goal2, 'keep') then {Set_Medication_Request(?action2, 'order') and ?goal1.satisfied ← 'no' and Assert(Is_Unsatisfied(?goal_forest))}

f. //Get user preference regarding unsatisfied goal
If (β and Is_Part_Of(?goal1, ?guideline1) and Is_Action_Inconsistent (?action1,?goal1, ?action2, ?goal2, ?log) and (?goal1.satisfied = 'no'))
⇒ If (User_Preference(?goal1, 'cancel'))
then ?goal1.status ← 'cancelled'
else If (User_Preference(?goal1, 'rerun')) then {
⇒ Activate_Guideline(?goal1, ?guideline1) and
⇒ Insert_PROforma_Data(?action2, ?guideline1) and
⇒ Run_PROforma_Guideline(?guideline1, ?goal1)
and ?guideline1.state ← 'build goal tree'

Sequence diagram of interactions

Control rules (d) and (e)

Control rule (f)